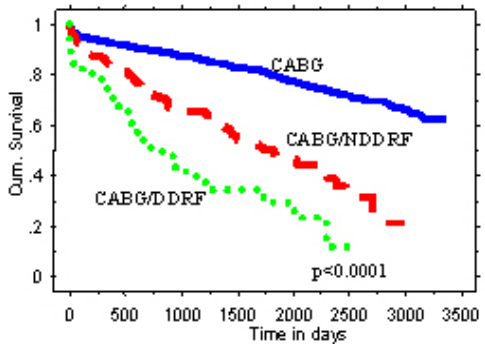
Noon

809-5 **Poor Outcome in Subsets of Renal Failure Patients Undergoing Coronary Artery Bypass Surgery: Mortality Results From a Cohort of 4,069 Patients**

Saida Zen Campwala, Ramdas G. Pai, Loma Linda University Medical Center, Loma Linda, CA

Background: Renal failure increases mortality in CABG patients. We studied the effect on mortality of renal failure (creatine>2mg/dl) - both non-dialysis dependent (NDDRF) and dialysis dependent (DDRF) - in high risk subsets of CABG patients.
Methods: This is a retrospective cohort study of 4069 consecutive adult patients who had CABG from 1993 to 2002. The mortality data was obtained from the National Death Index.
Results: The patient characteristics: age 67±12 years, men 73% and LV ejection fraction (EF) 49±16%. Over 3.9 years, 899 (22%) patients died. There were 3796 patients with normal renal function, and 273 (7%) with renal failure: 201 (5%) NDDRF and 72 (2%) DDRF. Patients with renal failure had a 5-year mortality of 56%, compared to 22% in patients with normal renal function (p<0.0001), with 50% in NDDRF, and 70% in DDRF. When corrected for the differences in the populations, both NDDRF and DDRF were independent predictors of mortality. In subset analysis, the 5 year mortalities in NDDRF and DDRF patients were even higher in patients with LVEF ≤40% (59 and 74%)}, age ≥65 years (60 and 70%) and redo-CABG status (64 and 100%). Besides renal dysfunction, LV dysfunction, advanced age and redo-CABG status were independent predictors of mortality.
Conclusions: 1) CABG patients with renal failure have a >50% mortality at 5-years, being higher in DDRF patients 2) In renal failure patients, LV dysfunction, advanced age, and redo-CABG status increase the 5 year mortality to prohibitive levels.



POSTER SESSION

1078

Myocardial Revascularization

Monday, March 08, 2004, Noon-2:00 p.m.
Morial Convention Center, Hall G
Presentation Hour: 1:00 p.m.-2:00 p.m.

1078-89 **Stem Cell Mobilization With Granulocyte Macrophage-Colony Stimulating Factor Has No Effect on Infarct Size and Left Ventricular Function in an Experimental Model of Acute Myocardial Infarction**

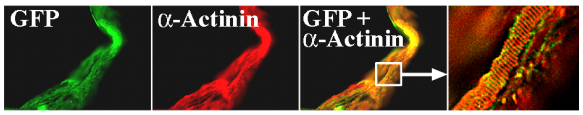
John Terrovitis, Apostolos Papalois, Christos Charitos, Paraskevi Dolou, Aggeliki Eleftheriou, Efstratios Charitos, Michail Mponios, Panagiotis Glentis, John Nanas, University of Athens School of Medicine, Athens, Greece

Background: Stem-cell therapy appears a promising treatment for cardiac repair in experimental and small-scale clinical studies in the setting of acute myocardial infarction (AMI). However, bone-marrow aspiration and in-vitro expansion of the desired cell lines are time-consuming techniques, impractical for implementation during an acute event. e sought to evaluate the effect of bone-marrow pluripotent stem-cell mobilization with GM-CSF on infarct size and left ventricular function in AMI, with a protocol easily applicable in everyday clinical practice. **Methods.** Ten pigs weighing 30 ± 5 kg were subjected to left thoracotomy and occlusion of the left anterior descending coronary artery for 1 hour, followed by reperfusion. At 50 minutes of ischemia, the animals were randomized to placebo (Group A, n=5) or GM-CSF (Group B, n=5). Subsequently, the thoracotomy was closed and the animals recovered. In Group B, 20 μg/kg GM-CSF (molgrastim) was administered subcutaneously, daily, for 15 days. All animals underwent echocardiographic evaluation at 5 and 28 days after AMI. At 30 days, they underwent a new thoracotomy and determination of the infarct size as a percentage of the whole left ventricular area (with the use of tetrazolium chloride). **Results.** No difference was observed between the two Groups in infarct size (7.8 ± 6.1 % vs 7.5 ± 7.7 %, p= 0.951, for Groups A and B, respectively). There was also no difference in shortening fraction (short axis view at the mid-papillary level, 34 ± 0.6 % vs 35 ± 0.5 %, p= 0.907), left ventricular end diastolic diameter (32 ± 0.2 mm vs 34 ± 0.3 mm, p= 0.361), left ventricular end systolic diameter (21 ± 0.2 % vs 22 ± 0.4 mm, p= 0.584) and systolic thickness of the infarcted left ventricular wall (0.97 ± 0.2 mm vs 0.98 ± 0.2 mm, p= 0.972), in Groups A and B, respectively at 28 days of follow-up. **Conclusion.** Subcutaneous administration of GM-CSF in the acute phase of acute MI and early post-infarction period does not result in either a decrease in infarct size or an improvement in LV function. Other protocols for adequate stem-cell mobilization and concentration in the injured area should be determined in order to combine efficacy and clinical applicability.

1078-90 **Epidermal-Derived Progenitor Cells Engraft the Infarcted Myocardium and Express Cardiomyocyte Markers**

Satyavardhan Pulukurthy, Ryan P. Dunlay, Timothy E. Lindley, Sarah J. Bonner, Christopher C. Oberley, Ram V. Sharma, Martine Dunnwald, Robin L. Davisson, University of Iowa, Iowa City, IA

Background: Lack of efficient regenerative capacity of the post-infarcted adult heart has prompted an intensive search for alternative sources of cells capable of repopulating the injured myocardium.In this study, we tested the hypothesis that skin-derived epidermal progenitor cells (EPCs) can engraft and express cardiomyocyte markers when transplanted into areas of myocardial infarction (MI).
Methods: EPCs were isolated from the epidermis of green fluorescent protein (GFP^+) transgenic C57 mice. Host non-transgenic C57 mice were given MI via open-chest left anterior descending coronary artery ligation. At the time of MI, GFP^+ EPCs or saline were injected at 2 sites near the infarct zone. Mice were sacrificed at 1, 3 and 6 weeks and immunofluorescence was performed on heart sections to detect GFP, cardiac, and epidermal cell markers.
Results: As early as 1 week post-injection, GFP^+ cells were engrafted in the infarcted region of EPC-injected hearts and co-expressed markers for differentiated cardiomyocytes (MHC, α-actinin). Over 6 weeks, GFP^+ cells gradually took on morphological features of adult myocytes including striated myofibrils (figure below). This was accompanied by a loss of the epidermal marker keratin 14.



Conclusion: Epidermal-derived progenitor cells engraft the infarcted myocardium to repopulate lost cardiomyocytes. The abundance, accessibility, and autologous nature of the skin may provide an exciting new therapeutic strategy for MI.

1078-91 **Transdifferentiation of Mesenchymal Stem Cells Into Cardiomyocytes by Direct Cell-to-Cell Contact With Nenatal Cardiomyocytes but Not Adult Cardiomyocytes**

Jihyun Yoon, Seung-Cheol Choi, Do-Sun Lim, Korea University Medical College, Seoul, South Korea

Background: Recent studies have demonstrated that direct cell-to-cell interaction is one of microenvironment factors for transdifferentiation of adult stem cells into cardiomyocytes. We investigated whether transdifferentiation of MSCs into cardiomyocytes was dependent on developmental stages of cardiomyocytes cocultured, and direct cell-to-cell interaction was essential for transdifferentiation. **Methods and Results:** MSCs were isolated from adult rat and cocultured in four different ways; 1) with neonatal cardiomyocytes, 2) with adult cardiomyocytes, 3) with neonatal cardiomyocytes on the cell culture inserts (double chamber system), 4) with the conditioned medium from neonatal cardiomyocytes. After 5 days of coculture with neonatal cardiomyocytes, 9.40±1.15% of DiI-labeled MSCs expressed sarcomeric-α-actinin as measured by flow cytometry. Immunocytochemistry showed that only these MSCs expressed the cardiac markers. MSCs transdifferentiation was not observed with other coculture condition as well as conditioned medium. Calcein-AM labeling of cardiomyocytes showed gap junctional communication between 56.1 ± 2.0 % of MSCs (24 hours after labeling, n=5) and neonatal cardiomyocytes. When MSCs cocultured with paraformaldehyde-fixed neonatal cardiomyocytes, they also expressed sarcomeric-α-actinin. EDTA abolished the adhesion of MSCs to fixed neonatal cardiomyocytes. **Conclusions:** These findings suggest that MSCs are capable of differentiating into cardiomyocytes when directly cocultured with neonatal cardiomyocytes by cell-to-cell interaction, but not with adult cardiomyocytes or with conditioned medium. This finding provides the model to study the mechanism to differentiate MSCs into cardiomyocytes by microenvrionment.

1078-92 **Human Umbilical Cord Mononuclear Cells Limit Acute Myocardial Infarction Size**

Robert J. Henning, Hamdi Abu-Ali, John Randolph, Michael Morgan, John Balis, Alison Willing, Paul Sanberg, University of South Florida, Tampa, FL, James A. Haley VA Hospital, Tampa, FL

Background: We hypothesized that Human Umbilical Cord mononuclear Blood Cells (HUCBC) can limit acute myocardial infarction size and improve cardiac function.
Methods: Infarction was produced in rats by either left anterior descending coronary artery permanent occlusion (n=35) or occlusion for one hour then reperfusion (n=36). Rats from each study were combined because of similar findings. Group 1 consisted of 24 control rats with no intervention. In Group 2 (n=33) the hearts were infarcted but no HUCBC injected. In Group 3 (n=38) one million HUCBC were injected at the ischemic zone edges 1 hour after coronary ligation. Immunosuppression was not given to any rat. Echocardiography was performed at baseline and at 1, 2, 3 and 4 months of observation.